

**REMARKS**

Applicants respectfully requests that the amendments to the claims be entered even though proposed after final rejection. The amendment to claim 1 simply deletes alternative embodiments from the claim. It is now required that the indicator be generated from the analyte by reagents present in the reaction mixture and that the indicator physically interact with the light-emitting moiety to inhibit light emission. Accordingly, claims 2-3 and 5-10 have been canceled, as inconsistent with claim 1 as amended. Claim 11 has also been canceled as now redundant with the limitations already in claim 1. Claim 12 recites a property of the indicator that was listed as an alternative in claim 1, but now, by virtue of the dependence of claim 12 on claim 1, is in addition to, rather than alternative to the requirement that the indicator physically interact with a light-emitting moiety. This duplication of properties provides for a dual function as the light-absorbing property will permit extension of the range of the assay.

What applicant has done, therefore, is to limit the invention to those embodiments where an indicator that physically interacts with the fluorescent component – *i.e.*, the light-emitting moiety, and that is generated from the analyte by the reagents in the reaction mixture. As these possibilities were already present in claim 1, the amendment amounts to cancellation of subject matter rather than adding any new material that would require a new search or raising any new issues. Entry of the amendment is therefore respectfully requested.

Applicant has found that by supplying a moiety that physically interacts with a light-emitting moiety to inhibit light emission, extremely low concentrations of substrate can be measured. This is illustrated in the application in the measurement of glucose in Table 3 which permits assay of quantities of glucose as low as 0.1 mg/dl and is able to generate results in a range between 0.1 and 0.125 mg/dl. As noted, no yellow color is visible in this range – *i.e.*, there is no discernible

light absorption. Thus, the indicator is behaving as required by the claims and is able to provide considerable sensitivity to the assay. As noted in the specification, this assay is approximately 1,000 times more sensitive than the colorimetric assay provided by Sigma.

The claims as previously pending were rejected as assertedly anticipated by Morris, US 5,173,434. While applicant does not believe that the prior claims were anticipated, for reasons that will be outlined below, it appears clear that as now limited, the claims are not anticipated by Morris. As noted by the Examiner, Morris teaches fluorescence quenching – *i.e.*, the emitted fluorescence wavelengths are absorbed by a substance which either absorbs light in the visible spectrum (quenching) or produces turbidity. The claims as presently proposed to be amended require that the indicator physically interact with the light-emitting moiety. This does not describe quenching or turbidity.

As noted above, Morris only discloses adding a fluorescent moiety or light-emitting moiety embedded in a matrix adjacent to the reaction mixture. It is not true, as the Office asserts, that the fluorescence emitter is “separated from the reaction mixture until the two are contacted and reacted together which must occur for the indicator to work.” This appears to imply that there must be a physical interaction between the fluorescence emitter and the light absorber in order for the light absorber to “work.” This is not the case – the light emitted travels over space from the external matrix to the absorber in the reaction mixture where it is quenched. There is no physical interaction required, and none occurs in Morris.

There is no disclosure in Morris of any instance where there is a physical interaction between the light-emitting moiety and the absorber of the emitted light.

In the previous action, the Office also called attention to a document cited in the background section of Morris, U.S. patent 4,495,293 to Shaffar. This patent indeed describes a fluorometric

assay in which a fluorescence emitter is in the same reaction mixture with a light absorber. This is described in the Summary of the Invention in column 3. Thus, the distinction previously drawn with regard to Morris as to the claims previously pending does not apply for Shaffar.

Nevertheless, from the description in Shaffar it is clear that the claims as proposed to be amended are distinct. As amended, the method requires that the indicator physically interact with the light-emitting moiety to inhibit light emission, as opposed to absorbing at a distance the light already emitted. That requirement for physical interaction is responsible for the enhanced sensitivity of the assay. As noted on page 4 of the specification, where this aspect of the invention is practiced, distinction can be made between glucose concentrations of 0.1-0.125 mg/dl. As shown in example 1 of Shaffar, in column 14, the glucose assay according to the quenching mechanism described is operable over a much higher concentration range of 0-300 mg/dl. Thus, neither Morris nor the referenced patent to Shaffar anticipate (or suggest) the present invention.

#### The Rejection Under 35 U.S.C. § 112, Paragraph 2

The objection to “the concentration” in claim 1 is, respectfully, believed to be misplaced. Simply because “the” is used, does not seem to applicant to mean that an *in haec verba* antecedent basis is required. In a sense, the antecedent basis is “an analyte” which must have some concentration, even if the concentration is 0. Thus, applicant believes that the inclusion of “the” is proper. If the Office prefers to change “the” to “a” or “any”, there is no serious objection. The objection to “if needed” in claim 1, to the format of claim 7, and to the asserted lack of antecedent basis of “the light” in claim 11 are believed moot in light of the amendments.

While applicant understands that certain headings and sections are suggested by the Office, it is not understood that these are required. Applicant has elected to use the section heading format employed in the Patent Cooperation Treaty and it is believed that this is proper.

The title of the invention has been changed to reflect the now proposed claims.

### Conclusion

The claims have been amended to limit the invention to one of the originally present three alternative embodiments – *i.e.*, that wherein an indicator physically interacts with a light-emitting moiety. This embodiment is clearly distinct from the disclosure both of Morris and of Shaffar. The objections made under § 112, paragraph 2, have been dealt with by amendment or explanation. Accordingly, it is believed that proposed claims 1, 4 and 12 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 527832000420.

Respectfully submitted,

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